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CLINICAL AND EPIDEMIOLOGICAL STUDIES ON RICKETTSIAL INFECTIONS.(U)

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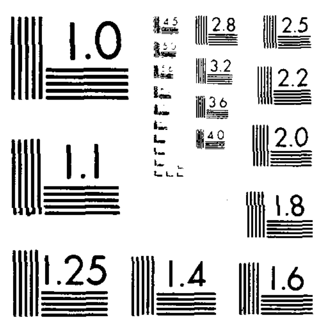

MICROCOPY RESOLUTION TEST CHART

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LEVEL II

CLINICAL AND EPIDEMIOLOGICAL STUDIES ON RICKETTSIAL INFECTIONS

ANNUAL REPORT.

Year-7(1979-1980)

By

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C. PROGRESS REPORT AND CURRENT STATUS

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PROGRESS REPORT AND CURRENT STATUS

1. BACKGROUND

a. The studies under the auspices of this Contact, reported herein, represent investigations currently or formerly undertaken with the collaboration or support of the following organizations— 1) In Ethiopia: Naval Medical Research Unit-5. 2) In Burma: Rodent Control Demonstration Unit/World Health Organization, along with the Ministry of Health of the Government of Burma. 3) In Egypt: Naval Medical Research Unit-3. 4) In Java: Plague Laboratory/World Health Organization. The joint projects with WHO were arranged with the support of Dr. Norman Gratz of the Division of Vector Biology and Control.

b. Essentially all of our time this year was spent in research on the ecology of murine typhus, and the findings continue to support our hypothesis that this rickettsiosis deeply involves: 1) indoor commensal murines or other small mammals (theraphions) which behave as a peridomestic species, such as Suncus shrews; 2) their ectoparasites such as fleas, lice and perhaps mesostigmatid mites and 3) hyperendemic minifoci or microfoci, wherein a large proportion of the commensal mammals and fleas and lice in a highly restricted locus, such as a single building (or even a rat-nest) are naturally infected with Rickettsia mooseri, the etiological agent of murine typhus.

c. In order to show how the data from the continuing studies in Burma complement and extend our earlier investigations in Ethiopia, we now summarize those results from the Ethiopian project.

1) The findings there strongly suggest that the following apply concerning R. mooseri infection in that country: (1) it is primarily associated with commensal Rattus (of which we collected only a single species), and not with campestral or sylvan rodents, or even indigenous murines anywhere; (2) it is centered in, or limited to, the indoors; (3) a variety of rat-ectoparasites are deeply implicated in the cycles, e.g. 3 species of fleas, 2 of lice (and possibly even mesostigmatid mites); (4) highly localized 'minifoci' exist, as in a single building, where an unusually high proportion of the resident Rattus, fleas and lice are naturally infected with R. mooseri and (5) the nest of Rattus in such a hyperendemic microfocus of murine typhus.

2) The data on the infection rates and some other points are summarized in Table 1, which is based upon results obtained with the indirect fluorescent antibody test (IFA).

	OUT-DOORS	IN-DOORS	NUMBERS	% POSITIVE	X. CHEOPIS	X. BANTORUM	L. SEGNIS	L. AETHIOPICA
I. AREAS WHERE RATTUS AND/OR MUS MUSCULUS ARE PRESENT								
A. RATTUS RATTUS								
1) ADDIS		+	118/190	60%	+	+	+	0
2) KOKA		+	3/105	3%	+	+	0	0
3) KOKA	+		0/1	-	+	+	0	0
4) INTOTO K. MEHRET		+	13/48	27%	+	+	+	0
5) TOTALS FOR RATTUS		+	134/344	39%				
B. MUS MUSCULUS		+	1/9	11%	+	+	+	0
C. MUS (LEGGADA)	+		0/4	-	+	+	0	+
D. PRAOMYS ALBIPES		+	3/118	2.5%	+	+	R	0
E. OTHER NATIVE RODENTS		+	0/52	-	+	+	R	0
F. OTHER NATIVE RODENTS	+		0/198	-	@	@	0	+*
G. TOTALS: ALL INDOOR RODENTS SAVE RATTUS AND MUS			3/170	1.8%				
H. TOTALS: ALL INDOOR RODENTS			138/522	26%				
I. TOTALS: ALL OUTDOOR RODENTS			0/208	-				
II. AREAS WHERE RATTUS AND MUS ARE PRESUMABLY ABSENT								
A. PRAOMYS ALBIPES		+	0/47	-	+	+	0	+
B. ARVICANTHIS	+		0/27	-	+	+	0	0
C. OTHER MURINES		+	0/39	-	+	+	0	+
D. OTHER MURINES	+		0/17	-	+	+	0	+
E. TACHYORYCTES	+		0/10	-	0	0	0	0
F. TOTALS FOR OUTDOOR RODENTS	+		0/54	-				
G. TOTALS FOR INDOOR RODENTS		+	0/86					

TABLE 1. SUMMARY OF DATA ON FA TESTS COMPARING RATES IN RATTUS RATTUS AND MUS MUSCULUS WITH OTHER RODENTS (INDOORS AND OUTDOORS) IN ETHIOPIA, WITH INDICATION OF THEIR MAJOR XENOPSYLLA AND LEPTOPSYLLA FLEAS (1975-1977)

Numerator = Number positive. Denominator = Number tested.
\+ = Present. 0 = Absent. @ = Does not apply to Tachyoryctes.
R = Rarely. * = Only on native "mice", etc.

3) From this table it is immediately apparent that R. mooseri was never demonstrated by fluorescent antibody (FA) tests of rodents in areas where Rattus (and Mus) were presumably absent, viz, no positives in 54 attempts from outdoor rodents, and 0/86 from indoors. In contrast, 60% of the samples (all indoors) from Rattus in Addis were positive, as were 27% from the nearby mountain village of Intoto. Including the Rift Valley site of Koka, where only 3/105 indoor rats were positive, the over-all R. mooseri rate for Rattus was 39%. Moreover, in the areas where Rattus was found, none of the 208 campestral rodents (Praomys, Arvicanthis, Desmomys etc.) were positive, but where some of these native murines shared quarters with Rattus, 3 of 118 Praomys were infected. The over-all rate for such indoor murines (excluding Mus and Rattus) in those areas was only 1.8%.

4) There was no significant difference observed in the rate of R. mooseri infection in female Rattus as compared to males, as shown in Table 2, and this was true regardless of the over-all rate of infection in an area.

LOCALITY	MALES		FEMALES	
	NUMBERS	% POSITIVE	NUMBERS	% POSITIVE
ADDIS ABABA				
Town	25/40	63%	27/45	60%
ADDIS SUBURBS (MAKANISSA)				
Village	7/11	64%	8/12	67%
Barn	16/20	80%	21/27	78%
ADDIS - MT. INTOTO				
Intoto Kedani Mehret	4/17	26%	8/31	26%

TABLE 2. MURINE TYPHUS INFECTION RATES BY SEX AND LOCALITIES AMONG RATTUS RATTUS COLLECTED IN ETHIOPIA (1976-1977)

Numerator = Number positive. Denominator = Number tested.

5) It would be expected that in an ectoparasite-borne infection, the oldest individual hosts would have the highest incidence of infection, since such rats obviously have had the maximum opportunity for acquiring the etiological agent. This picture was observed in Ethiopia regarding R. mooseri, as shown in Table 3. However, what is striking and important is that 1) the rate was already high in juvenile rats and 2) for 3 of the 4 observed foci, the difference between young and adult was only 11%-16%. Thus in Addis, 46%-53% of the juveniles tested already were positive for R. mooseri. The exception is noteworthy, for the incredibly high 91% infection rate in adults occurred in a single building, a barn, which surely must have been a hyperendemic minifocus. It is easy to imagine that in some parts of

the barn, perhaps in new hay, etc., there were a few nests that were free of infection, but that the young leaving such sanctuaries soon encountered the rickettsiae elsewhere in the barn when foraging for food.

LOCALITY	JUVENILES		ADULTS	
	NUMBERS	% POSITIVE	NUMBERS	% POSITIVE
ADDIS ABABA				
Town	8/15	53%	44/69	64%
ADDIS SUBURBS (MAKANISSA)				
Houses	4/7	57%	11/16	69%
Barn	6/13	46%	31/34	91%
ADDIS - MT. INTOTO				
Intoto Kedani Mehret Houses	2/10	20%	10/38	26%
TOTALS	20/45	44%	96/157	61%

TABLE 3. MURINE TYPHUS INFECTION RATES AMONG ETHIOPIAN RATTUS RATTUS BY AGE. (VICINITY OF ADDIS ABABA) (1976-1977)

6) Fleas as Potential Vectors of Murine Typhus in Ethiopia.

a) The data on Ethiopian fleas contributed markedly to our understanding of the ecology of murine typhus in that country. There is a rich fauna of fleas on Ethiopian rodents, especially in the highlands. Since the evidence we obtained on the laboratory and that in the literature (*#Traub et al, 1978) presumably exclude wild rodents and their ectoparasites as being of any real significance in the ecology of this rickettsiosis such fleas will not be discussed. Instead, we will review the main points about the fleas of commensal rodents in the areas we studied, but emphasize that in certain areas, native murines such as Arvicanthis, Praomys, Mestomys and Desmomys may enter huts or houses and act like peridomestic rodents. When they do, they occasionally may be found naturally infected with R. mooseri, or carrying an indigenous species of flea like Ctenophthalmus or Dinopsyllus, but generally they also are infested, to a degree, with the fleas found on Rattus locally.

b) It is important to note that the putative vector, Xenopsylla cheopis is found on Rattus indoors in the highlands and in the Rift Valley, and that a closely allied species, X. bantorum, of unknown significance in the infection likewise infest such rats. However, it is highly noteworthy that in certain areas both of these Xenopsylla are far more common on native murines living outdoors than on Rattus (which we reiterate were essentially restricted to the indoors in our study-sites if they were present at all). In this connection we emphasize that X. cheopis apparently arose in northern Africa and that Arvicanthis probably was its original host. Its association with commensal rats is secondary and probably occurred in relatively recent times (Traub, 1963 and 1972). Accordingly, the data we observed on the relative abundance of X. cheopis (and X. bantorum) in Ethiopia are not surprising.

c) Table 4 summarizes our observations on the prevalence of, and host-relationships of, the pertinent species of fleas, and we stress that the data reported apply to the dry season in Ethiopia, a time when X. cheopis and X. bantorum are 10-50 times as abundant during the rainy season.

	RATTUS RATTUS			ARVICANTHIS			MASTOMYS			PRAOMYS		
	X.C.	X.BA.	LE.S.	X.C.	X.BA.	LE.S.	X.C.	X.BA.	LE.S.	X.C.	X.BA.	LE.S.
I. ADDIS ABABA (2300-2500m) 1. Town (Bldgs.)	0.3	0.5	6	x	x	x	x	x	x	x	x	x
2. Suburbs	0.3	1	8	(--Field---) 0	0	0				x	x	x
3. Mountain Huts	0.2	0.2	7	0	0	0	x	x	x	0.1	0.2	1
II. KOKA-RIFT VALLEY (1640m) 1. Domiciles	1.0	1.5	0	50	6	0	3	15	0	x	x	x
2. Fields	x*	x	x	45	5	0	4	16	0	x	x	x
III. LEMI etc. (2600m) 1. Domiciles	x	x	x	x	x	x	1	2	0	0.1	3	0

TABLE 4. FLEA INDEX (AVERAGE NUMBER OF FLEAS PER HOST) FOR FOUR KINDS OF RODENTS IN VARIOUS AREAS AND HABITATS IN ETHIOPIA (1976-1977)

X.C. = Xenopsylla cheopis. X.BA. = Xenopsylla bantorum. LE.S. = Leptopsylla segnis.
x = Host does not occur here. 0 = Species of flea apparently absent.
Blank = No data. * = All Rattus were collected indoors except for 1 rat in Koka.

d) From this table, it is clear that while both species of Xenopsylla were found on Rattus in the Addis area and the Rift Valley as well, they were not abundant on that host. Thus, the maximum observed index never exceeded more than 0.3 X. cheopis and 1 X. bantorum per Rattus, whereas at the Rift Valley X. cheopis was 45-50 times as abundant on Arvicanthis in the adjacent fields than on Rattus (all indoors) and thrice as common on Mastomys. The corresponding figures for X. bantorum were: 3-16 times as prevalent. We believe that in the highlands, (and Addis Ababa is at 2400m. elevation), X. cheopis, like Rattus, is close to the survival limit regarding low temperatures. The observed discrepancy between the index on Rattus versus Arvicanthis at Koka, at 1640m., then seems even more anomalous and significant. It should be noted that 1) both of these Xenopsylla were present on Praomys and Rattus in huts at 2500m., but at very low population levels. In the Addis area, there was a third species found on Rattus, namely Leptopsylla segnis, and this was essentially restricted to that host, and was 7-9 times as prevalent on that host than either of the Xenopsylla. L. segnis, however, was not found in the Rift Valley.

e) By means of the direct fluorescent antibody test (FA), all three of these species were found naturally infected with R. mooseri, and all of the positive fleas were from Rattus, even though a total of 177 of those fleas from other hosts were dissected and tested. (In addition, 264 of other kinds of fleas were tested and all were negative, including 90 Echidnophaga from Rattus). The results of FA tests with the Xenopsylla and Leptopsylla segnis from Rattus are summarized in Table 5.

	XENOPSYLLA CHEOPIS	XENOPSYLLA BANTORUM	LEPTOPSYLLA SEGNIS
ADDIS ABABA TOWN & SUBURBS	3/59 5%	8/81 10%	61/323 19%
ADDIS MOUNTAINS	0/14	0/18	8/178 4%
KOKA RIFT VALLEY	0/49	0/61	
TOTALS	3/122 2%	8/160 5%	69/501 14%

TABLE 5. NUMBERS OF RATTUS FLEAS POSITIVE FOR R. MOOSERI INFECTION IN ETHIOPIA BY DIRECT FA TEST (1976-1977)

f) These results suggest that because L. segnis: 1)is a major parasite of Rattus; 2)is far more common on that host in Addis than either species of Xenopsylla and 3)has a higher rate of infection with R. mooseri in Addis than do the others, it may be a potent factor in the ecology of murine typhus. As we have pointed out, the possible role of L. segnis has been depreciated on the grounds that it presumably does not bite man, etc. (*#Traub et al, 1978), but if, as we believe, infected flea feces may be a potent source of infection in man and rodent, then the significance of L. segnis needs re-evaluation. This species may perhaps also be important as an intramuric vector. However, L. segnis cannot be an essential component of the R. mooseri cycle because the infection exists in areas where this flea is absent, namely the Rift Valley, and Burma, as we indicate below.

7) Rat Lice and R. mooseri in Ethiopia

a) The possible involvement of Rattus-lice in the ecology of this rickettsiosis has also been belittled for the same reasons as L. segnis, but here too we believe the question should be reconsidered in the light the possiblity of 1) dust-borne louse feces and 2) the relatively high rate of natural infection observed in Polyplax spinulosa and Hoploplura oeniomydis lice in Ethiopia. Out of 109 lice examined from Rattus in the Addis area, 7 (6%) were positive, namely 4 Polyplax and 3 Hoploplura.

8) Hyperendemic Microfoci of Murine Typhus

a) One of the most notable results of the program in Ethiopia was the evidence that hyperendemic foci of this rickettsiosis existed in highly localized areas or "minifoci" (e.g., a single building) in the Addis Ababa area. For example, in a dairy barn, the Rattus had a 79% infection rate (37/47) by IFA and in a domicile in town 74% (25/34) were positive. Not only were the infection rates in both rats and ectoparasites significantly higher in those loci than in other locations in the vicinity, but it was obvious that multiplicity of infection i.e., simultaneous occurrence of R. mooseri in Rattus and/or one or more kind of ectoparasite, was a concomitant and characteristic feature in such foci. This is shown in Table 6, which is based upon 12 Rattus and their fleas and lice, and in which 9 (75%) of the rats were positive for R. mooseri, as were 8 of 15 (53%) of the X. bantorum, representing 5 pools; 3 of 9 (33%) X. cheopis (4 pools); 20 of 63 (32%) L. segnis (11 pools); 2 of 36 (6%) Polyplax spinulosa (7 pools) and 1 of 8 (13%) of Hoploplura oenomydis (6 pools)

(TABLE 6, REFER TO NEXT PAGE)

INFECTION WITH R. MOOSERI

IN RATTUS	IN ONE SPECIES ECTOPARASITE	IN ANOTHER SPECIES OF ECTOPARASITE	NUMBER OF SUCH OCCURRENCES
+	+	+	4
+	+	0	5
0	+	+	2
0	+	0	1

TABLE 6. SIMULTANEOUS INFECTION WITH R. MOOSERI IN HOST RATS, XENOPSYLLA OR L. SEGNIS FLEAS OR HOPLOPLEURA OR POLYPAX LICE (ETHIOPIA)

Thus, in four instances, the Rattus and at least two species of fleas or lice present on those rats were positive by FA, and in 5, both rat and one species of ectoparasite had evidence of R. mooseri infection. On two occasions, representatives of three species of fleas found on the individual rats were positive. Moreover, if one member of a species of ectoparasite in the pool harbored R. mooseri, then most of the specimens in the pool were also positive, e.g. in 13 of 23 pools which had any infected individual lice or fleas, more than 39% of the representatives of that species of ectoparasite in the pool had R. mooseri. Once, every member tested for 3 species of fleas from an individual rat were infected, and in another example, 100% infection was noted for one species of fleas from these areas, there were 17 rats which carried positive fleas or lice, but where only one or the other of these kinds of ectoparasites were tested. Here 15 (88%) of the rats were seropositive, and 13 carried L. segnis, of which 57% of the 89 tested were positive by FA. Four rat-lice were tested (one from each of four hosts) and all had R. mooseri.

b) From these observations it seems quite clear that when an individual louse or flea became infected, a significant proportion of the other lice or fleas on that rat also acquired R. mooseri. These findings suggest that either the host had a pervasive rickettsemia at the time (and rickettsiae are present in the blood of the rat only for a few days) or else there was a plethora of rickettsemic hosts available in that focus during the lifetime of the fleas and lice. Even more striking are the facts that 1) of the 29 rats mentioned above, 22 (76%) came from either of two buildings and 2) both of these sites produced such high rates of infection during two field trips one year apart, e.g. 83% and 76% in rats in the barn and 78% and 77% in the house in town. Such impressive persistence of infection in a locus is significant and immediately suggests dust containing feces of infected ectoparasites as a source because it is known that dried flea feces can remain infective for years (*#Traub et al 1978). Such dust would be concentrated in the nest. Another possible explanation for the persistence would be continuing cycling of rickettsiae between hosts and arthropod vectors, but this too would be most likely to be effected within the nest, with the progeny becoming infected before they are old enough to disperse. These observations on multiple infections, persistence etc., coupled with that on the surprisingly high rate of infection in juvenile rats (Report p4 above) all suggest that the actual site of the rickettsial exchange is in the Rattus nest, which thus would be a veritable hyperendemic microfocus. This concept is also suggested by the observations reported in the next paragraph.

9) Murine Typhus as an Indoor Infection in Ethiopia

There has been no hint that rodents collected or living in the outdoors, or their ectoparasites, are in anyway involved in the ecology of murine typhus in Ethiopia. In contrast, 138 of 865 murines collected in buildings had been infected by R. mooseri as indicated by IFA tests, and all the FA-positive ectoparasites came only from indoor hosts. However, since more than 97% of the IFA-positive rodents were Rattus, and 99% of the Rattus came from within buildings[@], it might be concluded that the fundamental relationship was with Rattus per se. and not the indoor environment. Such a deduction is reinforced by the observations that 1) the remaining few murines found infected (i.e., 3 Praomys and 1 Mus musculus) were living in buildings simultaneously occupied by Rattus and 2) Praomys and other native murines were uniformly negative when from areas where Rattus did not occur (e.g., at Lemi and Menagesha), even if such indigenous rodents were trapped within domiciles. Now there can be no doubt that, in Ethiopia at least, Rattus plays a fundamental role in the cycles of murine typhus, but the association with the indoors seems inherent as well. Thus, Praomys, like Desmomys, Arvicanthis and Mastomys, freely enter and leave huts, generally carrying their own Ctenophthalmus, Chiastopsylla and Dinopsyllus fleas, but at times harboring Xenopsylla cheopis and X. bantorum. (It will be recalled that at Koka, in the Rift Valley, Arvicanthis and Mastomys had 10-20 times as many X. cheopis and X. bantorum. as did Rattus in the same area.) It may seem that some of the native murines would acquire R. mooseri infection (as the 3 Praomys did at Intoto in the mountains a few miles from Addis) and transmit it to their associates outdoors and establish it there, but, for example we have no evidence of R. mooseri in Arvicanthis trapped just a few feet from the hyperendemic barn in the Addis suburbs, or in the Xenopsylla-ridden Arvicanthis and Mastomys at Koka. We have shown that Arvicanthis is experimentally susceptible to R. mooseri., "Natural immunity" is therefore, not the issue. Some factor is missing, and we believe the environment in the Praomys, Mastomys or Arvicanthis nest is different from that of Rattus even if the former three may nest indoors (and we don't know if they ever do, in those

FOOTNOTE
@ In other parts of Africa, commensal Rattus are found in gardens and fields as well as in buildings. It is not clear whether the restriction of Rattus to the indoors in our study-areas is because the group has been only relatively recently introduced into Ethiopia, or because of unfavorable external conditions, e.g., the cold temperatures in montane regions like Addis Ababa and the aridity in the Rift Valley (or a combination of both factors). It should also be noted that in Ethiopia the only Rattus we collected was R. rattus.

areas). For example, while Rattus, Praomys, and Desmomys may be trapped in the same hut at Intoto, there is very little exchange of fleas. We have never taken Ctenophthalmus etc. from Rattus, and only very rarely have seen Leptopsylla on Praomys. Further, the Rattus rattus were nesting in the roof, and the others were found only on the ground, further suggesting little contact between the commensals. These observations, limited as they are, likewise are in accord with a hyperendemic focus in the nest of Rattus, and in the Ethiopian loci, this is in the indoors.

10) Data from Mesostigmatid Mites and Ticks

No evidence of R. mooseri infection was found in mesostigmatid mites or ticks in our Ethiopian project. However the sampling was very small and included only 205 mites from Rattus, and no ticks were collected from that host. The methodology was not at fault, since spotted fever-group rickettsiae were successfully demonstrated in mites and ticks from non-Rattus hosts.

2. RESULTS OF STUDIES IN YEAR 06

a. Investigations in Baltimore

1) All the microbiological and serological work done in support of the overseas operation is carried out in our laboratory in Baltimore (and much of this is achieved at no expense to the Contract). Some of the basic research being done in the Department under other auspices is also an integral part of the program on murine typhus, e.g. the thesis of Silvio Arango-Jaramillo on the natural history of murine typhus in the rat. Since the findings on the development and persistence of rickettsiae in the blood and on antibodies following experimental infection, and those of our other laboratory studies contribute directly to the understanding of the ecology of murine typhus, those results are now summarized before discussing the studies in Burma.

2) It was found that the laboratory rat is extremly susceptible to infection with R. mooseri, viz. inoculation, through the skin, of an estimated 1-2 viable organisms was capable of infecting 50% of the rats. Such an infection, however, remained inapparent and did not produce detectable illness or death. In both adult and newborn rats rickettsemia appeared about one week after inoculation and lasted for about one week. The rickettsiae could be detected in kidneys and brains for 28 days after inoculation, but could not be demonstrated on the 35th day (although they perhaps may persist in other tissues or could be detectable by some techniques yet unknown). There was no evidence of transplacental infection. Antibodies against R. mooseri appeared in the blood about 10 days after inoculation and persisted for a minimum of 91 days (i.e., presumably for virtually the entire life-span of the host). Newborn rats apparently responded immunologically to the infection in the same manner as the adults, i.e. the antibody response and

effective control of the infection were similar. This was true even if inoculated on the first day after birth (*#Arango-Jaramillo et al A, in prep.).

3) In those studies it was also observed that maternal anti-R. mooseri antibodies were transmitted to the progeny primarily through the colostrum and milk, but declined precipitously after the 18th postnatal day. Baby rats born of mothers with high antibody titers, and acquiring such passively transferred maternal antibodies nevertheless developed a primary type infection when the maternal antibodies had fallen to undetectable levels, i.e., they responded in the same manner as a rat that had never been exposed to infection or ever had antibodies. (*#Arango-Jaramillo et al, B, in prep.). However, it is not yet known whether the passively-acquired antibodies do actually protect the infantile rats against infection, or if they prevent rickettsemia or if they merely ameliorate the course of the infection.

4) Our other new studies have shown that X. cheopis fleas were remarkably efficient in acquiring and maintaining R. mooseri infection - viz, 100% of the X. cheopis that fed on rickettsemic baby rats were positive by FA 4 days after feeding, and 100% the samples tested on 30 days post infective-feeding were also positive, emphasizing the striking ability of these fleas to retain the infection without a reduction in longevity. Such effects might be expected in the putative vector, X. cheopis but, significantly, Leptopsylla segnis gave identical results, reinforcing our argument that the vector-capacity of this latter species merits serious study.

5) Certain aspects of this preliminary research on rickettsia-host-flea inter-relationships are yet to be resolved, e.g. the degree of protection maternal antibodies provide baby rats. Thus, no studies have been done anywhere on the course of R. mooseri infection in baby rats which have substantial titers of passively acquired maternal antibodies. Similarly, we assume, but have not yet proven, that L. segnis and X. cheopis whose intestinal cells are invariably loaded with R. mooseri 30 days after feeding on a rickettsemic rat, are truly infective and are voiding, virulent rickettsiae with their feces. Nevertheless, the laboratory findings to date strongly support our hypothesis of the rodent nest as a hyperendemic microfocus of R. mooseri infection. Thus; 1) baby rats are highly susceptible to infection, even if born of an infected mother. 2) Very young rats produce a relatively long-lasting period of rickettsemia - the same as adults - from about 10 days after infection with only 1-2 rickettsiae, until about the 17th or 18th day. This is surely long enough to infect large numbers of fleas which abound in such nests, and which readily acquire the organism even after only one night's exposure, and maintain them in the gut for at least a month. 3) The infected infantile and young rats are not noticeably adversely affected by the rickettsiae. 4) There is no mortality or epizootic to reduce the numbers of "reservoirs" or sources of infection to other rodents and ectoparasites. 5) Even if the newborn rats were effectively protected by the passively acquired maternal antibodies, that defense mechanism would not prevent infection before the young were old enough to disperse from the nest.

b. Data and Observations Based Upon the Studies in Burma

1) Incidence of Murine Typhus Infection in Man in Rangoon

a) Although our collaborative project with RCDU etc. had clearly demonstrated that murine typhus infection was common and widespread in commensal theraphions in the Rangoon area, and presumably in their fleas and lice as well, there was no information available as to whether there was a concomitant problem regarding human health. Accordingly, during our field trips, introductory steps were initiated to obtain data on the incidence of murine typhus in man, and the preliminary results are summarized below.

b) By direct clinical study, the Responsible Investigator showed that a significant proportion of hospitalized cases diagnosed as "pyrexia of unknown origin" actually had murine typhus, at the time. It was also clear that such cases were probably common and unrecognized due to lack of awareness of the problem and the absence of suitable means of diagnosis.

c) In order to assess the potential significance of murine typhus as a human medical problem in Rangoon, a serosurvey was organized and executed as a joint project between the Government of Burma, the World Health Organization and our Department, with all the laboratory testing performed in Baltimore. The data are still being accumulated and studied, but the preliminary results, summarized below, are fraught with interest.

(1) To date, about 22% of all the people surveyed (by IFA tests) show evidence of having been infected with murine typhus sometime during their lives. Overall, as well as when grouped by decades according to age, there was no significant difference in the rates for males and females, apparently indicating that both sexes were equally at risk. This observation suggests the possibility that the infection was acquired at home rather than in the fields or at work. It also seems that 1) below the age of ten, about 11% of those tested were positive; 2) between the ages of 20-40, about 25%-30% of the population tested were infected and 3) by age 50, the level of incidence of infection was approximately 35%. Thus half of the population with antibodies were already positive by age ten, and this too suggests a domicilary source of infection.

(2) At this stage of the survey, possible error regarding skewing due to limited sampling cannot be excluded, but it appears that the type of housing the people resided in may have had an effect on the incidence of murine typhus in the occupants. Surprisingly, there was an observed higher rate in people who lived in modern, cottage-type homes as compared to residents of 1) traditional thatched houses which are mounted on stilts, well above ground level and 2) flats in large, tenement-type of buildings. If this turns out to be a statistically valid observation on the basis of additional data now being studied, then it may be of importance in epidemiology and prevention. It would surely be expected that

infected rats were more common in the vicinity of the latter two types of domiciles than in or near contemporary Western types of cottages. However, actually there may be notably less direct contact with rats, ectoparasites and their feces and nests in the thatched hut and tenement than in the bungalow. For example, Rattus rattus generally nests in the roofs of domiciles, and in the newer style home in Rangoon this cannot be easily accomplished, and if these rats are thus forced to nest at ground level or in cupboards therein, the chances of exposure to the sources of infection may be enhanced. We are attempting to get more data on the incidence of murine typhus infection in man in the various types of domiciles and are examining the various factors and ramifications suggested above.

(3) Regardless, even the preliminary figures on incidence of murine typhus infection and disease in man support the concept that this rickettsiosis should be of definite concern to the public health authorities in the Rangoon area.

2) Murine Typhus Infection in Small Mammals and their Ectoparasites in Burma

a) Small Mammals (Theraphions) in the Rangoon Area

(1) The fauna of commensal theraphions in Rangoon is remarkable for its diversity and density. There are six species that are found in and around buildings. Of these, five are murine rodents: Rattus norvegicus; R. rattus; R. exulans; Bandicota bengalensis; and the house mouse, Mus musculus, while the sixth is an insectivore, the shrew Suncus murinus. All of these have been found, in our study, to be naturally infected with R. mooseri. A seventh species, Bandicota indica is at times found in or near buildings but is difficult to trap by the methods necessarily employed by RCDU and the few individuals taken were in fields, cemetaries etc. B. indica has been seropositive in our survey, but the sampling has been limited.

(2) When it is realized that conditions are extremely favorable for peridomestic rodents and shrews in Rangoon, and the reproductive potential of these mammals are reviewed as per Table 7, the enormity of the problems of rodent control and prevention of murine tyhus and plague, both of which occur in Rangoon, becomes readily apparent. Table 7, dealing with the reproductive patterns of the first 6 of these theraphions, was compiled by Dr. A. Farhang-Azad of our Department, based upon sundry sources and data from our colleagues at RCDU Rangoon.

(TABLE 7, REFER TO NEXT PAGE)

(3) From this Table it will be noted that the reproductive capacity of a single female ranges from 24 to 70, depending upon the species. The nigh-incredible figure of 70 for B. bengalensis applies to India; 40 is the corresponding number for Rangoon. Of particular interest to our thesis regarding hyperendemicity in nests are the categories of incidence of pregnancy (i.e., numbers of litters per annum) and the age of maturity. Thus, R. rattus would be expected to be in a nest with young 5 times a year, and Bandicota, 11. Many rats use their old nests for succeeding generations, thereby presumably compounding the chances for acquiring and transmitting the rickettsiae via ectoparasites and their

	RATTUS NORVEGICUS	RATTUS RATTUS	RATTUS EXULANS	BENDICOTA BENGALENSIS	MUS MUSCULUS	SUNCUS MURINUS
Gestation in Days	22-25	21-22	22-23	21-23	18-21	
Incidence of Pregnancy (per year)	4	5	6	11	8	3*
Age at Maturity	40 Days	40 Days	45 Days	--	35-42 Days	--
Percent Pregnant of Adult and Subadult	20%	25%	30%	52%	35%	59%
Average Litter Size	9*	5*-6	4	6-7*	5.5	10*
Post Partum Pregnancy	Yes	Yes	Yes	Yes	Yes	Yes
Production per Female per Year	36	31-38*	25-36*	40*-70	42	24*

TABLE 7. REPRODUCTIVE PATTERNS OF FEMALES OF CERTAIN COMMENSAL MAMMALS. (FROM VARIOUS SOURCES)

* = New Data applying specifically to Rangoon.

feces, of the fleas lice and mites. Also sometimes some of the young remain in the old burrows system and do not disperse to new sites. Where data are available, the rats are mature within a short period of time, and hence most are soon establishing their own nests and potentially hyperendemic foci.

(4) The observed rate of natural infection with R. mooseri in these commensal theraphions in the Rangoon area was impressively high (although not approaching the astonishing levels of Addis Ababa). As noted in Table 8, the rates were highest in Rattus norvegicus and R. rattus, with 30% and 27% respectively. There was little observed difference between the sexes regarding infection in any one species, except in the case of M. musculus, where sampling may be a factor. Where there was a difference, however, it favored the female, and perhaps this may reflect the greater period which that sex spends in the nest.

	TOTALS	MALES	FEMALES	YOUNG	ADULT
BANDICOTA BENGALENSIS	238/1575 15%	94/680 14%	147/895 16%	2/33 6%	237/1542 15%
RATTUS RATTUS	70/263 27%	24/104 23%	46/159 29%	0/15 -	70/248 28%
RATTUS NORVEGICUS	46/151 30%	22/78 28%	24/75 32%	3/11 27%	40/142 28%
RATTUS EXULANS	160/842 19%	48/272 18%	112/570 20%	38/217 17.5%	122/645 19.5%
MUS MUSCULUS	7/125 6%	1/53 2%	6/72 8%	-	-
SUNCUS MURINUS	154/960 16%	89/559 16%	65/401 16%	5/42 12%	149/918 16%

TABLE 8. RICKETTSIA MOOSERI INFECTION IN SIX SPECIES OF COMMENSAL MAMMALS IN RANGOON AND OTHER URBAN AREAS AS SHOWN BY INDIRECT FLUORESCENT ANTIBODY TESTS FOR 1975-1978.

Numerator = Number positive;
Denominator = Total number tested.

(5) The figures comparing the R. mooseri rate in young versus adult theraphions in Table 8 are worthy of note, for they are fully in line with the idea that the nest is a key focus of murine typhus infection. Thus, the percentage observed for young R. norvegicus is almost as high as for the adult, and the same is true for R. exulans, while the differential in the case of Suncus is likewise very small. Where there is adequate sampling, the maximum disparity was observed concerning B. bengalensis, and even here the rate in the young rats was more than 1/3 that of the adults. As for R. rattus, we believe the 0/15 observed for young individuals represents inadequate sampling.

(6) Only three Bandicota indica were tested, and two of these were positive by the IFA test. We hope to obtain more B. indica on the next trip.

b) Fleas and Lice

(1) Like the hosts themselves, all the fleas reported from the rats and Suncus in Rangoon are introduced species.

(2) Last year we presented data on the host relationships of Xenopsylla cheopis and X. astia, the two overwhelmingly dominant fleas on commensal theraphions in Rangoon, and showed that more than 80% of the fleas or Rattus exulans and Suncus murinus were X. cheopis and the remainder were X. astia. In contrast,

nearly 90% of the fleas on Bandicota bengalensis were X. astia and less than 10%, X. cheopis. On R. norvegicus, X. astia outnumbered X. cheopis by about 2:1 and only on R. rattus were the two species nearly equal in number (53% X. cheopis) Data that express these relationships in a different way, and which include extensive recent collections, are shown in Table 9. This compares the "index" for these two species, but they are tallied by whether or not their hosts were found to be positive for R. mooseri by FA tests.

(3) It must be stressed here that, because of the way the fleas were collected, the "index" cited probably does not give a true representation of the average number of fleas on these hosts at the time the mammals were trapped. Under the conditions the collectors in Burma must conduct their plague survey, which is the source of these collections, the animals remain in the traps in an excited state for hours before examination. Under such circumstances, many fleas leave their hosts (#Traub, 1972). Nevertheless, the Burma collections and procedures for examination were always made in standard and uniform ways, and hence the data are valid for purposes of comparing host-infestations. There is no doubt that X. astia is far more prevalent on B. bengalensis than is X. cheopis and the reverse is the case of the three species of Rattus and Suncus murinus, usually in the ratio of 3-8:1, essentially as shown in Table 9. X. cheopis was twice as abundant on R. rattus and R. norvegicus on the other hosts.

HOST	HOST + R. MOOSERI			HOST NEGATIVE		
	X. CHEOPIS	X. ASTIA	BOTH	X. CHEOPIS	X. ASTIA	BOTH
BANDICOTA BENGALENSIS	0.4	5.7	6.1	0.5	3.7	4.2
RATTUS RATTUS	0.2	0.5	2.5	1.1	0.5	1.1
RATTUS NORVEGICUS	2.0	1.7	3.7	2.0	2.4	4.4
RATTUS EXULANS	0.8	0.2	1.0	0.7	0.2	0.9
SUNCUS MURINUS	0.8	0.1	0.9	0.7	0.1	0.8

TABLE 9. FLEA "INDEX" (AVERAGE NUMBER OF FLEAS PER HOST) FOR FIVE SPECIES OF COMMENSAL THERAPHIONS FROM RANGOON AND OTHER URBAN AREAS IN BURMA (1977-1979)

(4) In the literature on murine typhus, the point has several times been made that, in general, rats which are serologically positive for R. mooseri tend to be infested with more fleas than are rats that are negative (*#Traub et al 1978). The explanation proferred has been that, on the whole, rats with a larger number of fleas have a greater chance of acquiring the infection. However, as we pointed out in that Review, the positive rat must have been infected at least 9 days before it acquired its present crop of Xenopsylla. Presumably, the rat with an unusually large number of fleas generally come from a microhabitat favorable for fleas (unless its "index" is due to special circumstances, such as having just been caught, etc.), and hence is more likely to have been exposed to R. mooseri in the past. Regardless, the data in Table 9 show that for four of the five hosts listed, the seropositive rats had a slightly greater number of fleas than did the normal hosts. However, we do not regard the difference as significant, either statistically or in implication.

(5) R. mooseri infection in Fleas, Lice and Mites from Rangoon.

(a) In the previous Report we stated that 43 (19%) of the 221 Xenopsylla from Rangoon tested by FA were positive for R. mooseri, as were 1 of 18 Ctenocephalides felis. In Table 10 we present data on the results with ectoparasites collected during our field trip in October, 1978, subsequent to the above records.

ECTOPARASITE	NUMBER EXAMINED	NUMBER POSITIVE	NUMBER POSITIVE
FLEAS:			
XENOPSYLLA ASTIA	850	54	6%
XENOPSYLLA CHEOPIS	196	19	10%
ECHIDNOPHAGA GALLINACEA	81	18	22%
CTENOCEPHALIDES FELIS	3	0	-
TOTALS	1130	91	8%
LICE:			
POLYPLAX SPINULOSA and P. RECLINATA	435	14	3%
HOPLOPLEURA PACIFICA	105	1	0.9%
TOTAL	540	1	3%
MESOSTIGMATID MITES (2 spp.)	184	17	9%
TICKS	2	0	-
GRAND TOTALS	1856	123	7%

TABLE 10. SUMMARY OF RESULTS OF DIRECT FLUORESCENT ANTIBODY TESTS OF ECTOPARASITE SMEARS TESTED FROM RANGOON, BURMA. 1978

(b) These data, involving a much greater number of fleas, indicate an 8% over-all infection rate for the 1130 fleas examined, with 10% and 6% of the X. cheopis and X. astia positive, respectively. The 22% rate for 81 Echidnophaga gallinacea is of special interest, since there are very few reports of natural infection for that species (*#Traub et al, 1978), and the percentage noted as infected in Burma is exceptionally high (even exceeding what we observed for fleas in Ethiopia). These stick-tight fleas came from a total of four B. bengalensis, and the high rate may be due to circumstance (e.g. a hyperendemic microfocus) rather than represent anything characteristic of the species of flea, host or locality. (Echidnophaga was negative in our samples from rats in houses in Koka, Ethiopia) More data are required.

(c) As can be seen from Table 10, both Polypax and Hoploplura lice were found naturally infected with R. mooseri. Of the species listed, only Polyplax spinulosa had been found in Ethiopia. Additional sampling, testing and data are required before any interpretation can be made of the results, other than to point out that once again rat lice are being incriminated to some degree, and reiterate that they should be studied further. Dust-borne particles of feces from infected rat lice may be a source of R. mooseri in man or rat.

(d) The present report of 17 (9%) infected mesostigmatid mites is one of the very few extant concerning this group of ectoparasites and encourage us to intensify our efforts in this regard. Mite feces must also be considered as potential consequence in the ecology of murine typhus.

(6) The Relative Importance of Certain Fleas and Hosts in the Ecology of Murine Typhus in Rangoon.

(a) Theorectically, certain of the fleas and theraphions may be more important in the ecology of this rickettsiosis than are the other species. Figure 1 was compiled to see if the data available at this stage of the project offer any such indication.

(FIGURE 1, REFER TO NEXT PAGE)

(b) The solid line for the percentage of infected hosts show the highest rates for (1) Rattus norvegicus and (2) Rattus rattus. Both of these hosts were infested with the largest number of X. cheopis, i.e. the "index" was at least double that of the other fleas listed. Bandicota bengalensis had more than tenfold as many X. astia as X. cheopis, and its IFA rate was 15% as compared to 27% for R. rattus and 30% for R. norvegicus. More data are required, especially from hyperendemic foci, but it appears likely that in Rangoon, X. cheopis and these two species of Rattus are more cardinal to the natural history of the infection than the other species. It will be recalled that in Ethiopia (where there were no R. norvegicus collected in our study areas) 1) all signs pointed to R. rattus as the key figure for R. mooseri and 2) X. cheopis was found whenever R. mooseri was demonstrated. However, there that flea could be common in areas and foci where R. mooseri was apparently absent. Also, Leptopsylla segnis, a species not reported in Burma, was far more common than

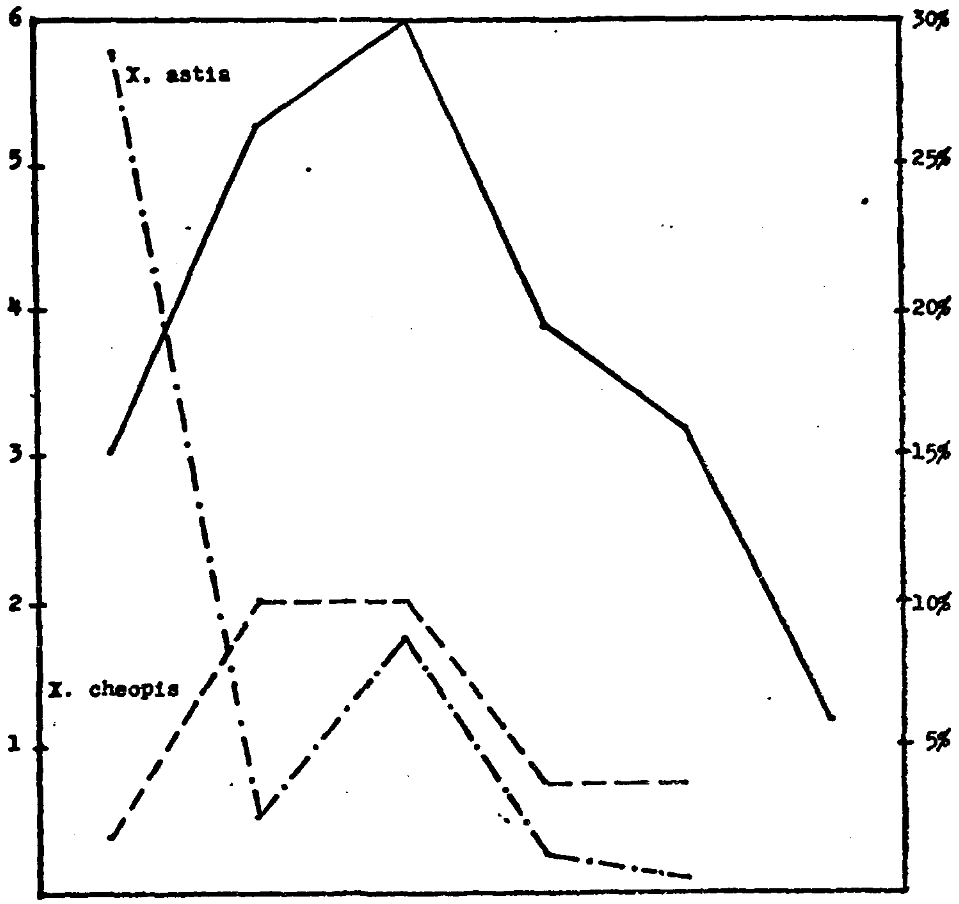

FIG.1. THE PERCENTAGE OF COMMENSAL HOSTS INFECTED WITH RICKETTSIA MOOSERI AS COMPARED TO THE FLEA INDICES FOR XENOPSYLLA CHEOPIS AND X. ASTIA ON THOSE HOSTS. (RANGOON AND OTHER URBAN AREAS IN BURMA, 1977-1979.)

than X. cheopis in Addis and was infected with R. mooseri at a higher rate, but L. segnis was unknown in the endemic focus at Koka in the Rift Valley. We mention this to indicate the complexity of the problem and stress the need for more data.

3) Murine Typhus Infection in Other Parts of Burma

a) It is of prime concern to the Burmese Government to learn the extent of the murine typhus problem in their country and we and RCDU/WHO were invited to extend our investigations well north of the Rangoon area, and to study conditions there in urban, rural, sylvan and campestral areas. Such an endeavor of course would also help obtain answers to basic and critical questions about the ecology of murine typhus, and we therefore hastened to comply to the limits of feasibility.

b) Among the unresolved questions are such points as: 1) whether this rickettsiosis occurs in the absence of commensal Rattus. 2) If so, what are the reservoirs and vector(s)? 3) Are there cycles involving purely sylvan and campestral theraphions, regardless of whether commensal Rattus are present? 4) If so, what are the major vectors? 5) Does Rattus norvegicus occur in towns and villages up-country, or is it limited to the main port areas, and perhaps to a limited extent along major roads, and railroads and rivers, as we had suggested in our Review (*#Traub et al, 1978) was the case for this rat?

c) Although RCDU has just started operation up-country and these have necessarily been on a limited scale, the still highly preliminary results are extremely interesting and promising, as shown in Table 11.

AREA	RATTUS RATTUS	RATTUS EXULANS	BANDICOTA BENGALENSIS
MYINGYAN	30/45 67%	0/4	1/2 50%
PEGU		1/1 100%	2/10 20%

TABLE 11. PRELIMINARY RESULTS OF IFA TESTS ON SOME RODENTS COLLECTED IN COLLECTED IN TOWNS IN NORTH OF RANGOON (1979)

(1) The exceptionally high rate of infection (67%) in the 45 Rattus rattus from Mingyan immediately calls for further study of that area, which is near Mandalay, several hundred miles from Rangoon. The absence of R. norvegicus in those collections, limited as they are, may prove significant. Pegu is a few miles north of Rangoon but the figures in Table 11 hint that the ecology of the infection may be somewhat different there.

4) The data and observations on murine typhus in Burma clearly indicate that this rickettsiosis is widespread and common in rodents, and, at least in the Rangoon area-the only place for which we have information as yet-the same is true for infection in man, shrews and the major ectoparasites of rats and shrews (Xenopsylla fleas and rat lice, and probably blood-sucking mites). The findings support the conclusions we reached in Ethiopia concerning 1) the cardinal role played by commensal Rattus and 2) the potential importance of the rat nest as a possible hyperendemic microfocus of R. mooseri infection. The need for further study along selected lines, and the importance of such investigations are amply indicated.

c. Studies on Zoogeography

1) Research on the faunal affinities and zoogeography of ectoparasites like fleas, lice and trombiculid mites have led to the demonstration of the occurrence of chigger-borne rickettsiosis and tick typhus in wholly unexpected geographical and

ecological areas, and have contributed significantly to our knowledge of the ecology and distribution of plague and murine typhus (#Traub and Evans, 1967, #Traub and Wisseman, 1968; 1974; *#Traub et al, 1978). The investigations on murine typhus in Ethiopia resulted in data on ectoparasites and rodents that greatly assisted in the preparation of a long article on the zoogeography and evolution of certain mammals, fleas and lice.(*#Traub, 1980, in press) Some of the conclusions deal with the distribution of some reservoirs and ectoparasite vectors of disease, and hence are pertinent. The abstract is therefore quoted here.

"Data on the zoogeography, phylogeny and evolution of fleas and lice support the concepts of austral faunal relationships, transatlantic connections and other aspects of the theory of continental drift. Primitive hosts tend to have primitive fleas and lice, while the most evolutionarily youthful ectoparasites are associated with the most advanced mammals. Fleas generally parasitize the hosts with which they evolved or else those which developed later, rather than infest hosts lower on the evolutionary scale. Primitive hosts and their fleas and lice tend to be conservative and change very slowly at the generic, or even species level, especially as compared to relatively recently evolved forms such as murids and their fleas. The close correlation between the kind of ectoparasite occurring on tetrapods and the geological time the hosts first arose extends to Class and Order, with only mites occurring as true parasites of Amphibia; mites and ticks on reptiles, etc., extending to a gamut of ectoparasites on rodents. Thus, hosts arising before the Paleocene lack Anoplura, e.g. the bats.

The Siphonaptera demonstrating southern affinities (e.g. stephanocircids, doratopsyllines, pygiopsyllids and pulicids) are the more primitive groups of fleas. The main families on the boreal continents (Ceratophyllidae and Leptopsyllidae) are essentially northern in distribution and are clearly more youthful in evolutionary development than the preceeding ones. The siphonapteran relationships among the austral continents are at the level of subfamily or family, not the genus.

The marsupials presumably arose in South America in the Late Jurassic or Early Cretaceous and dispersed to Australia, at least in the Early Cretaceous, via Antarctica, carrying stephanocircid and doratopsylline fleas and amblyceran Mallophaga. Other marsupial elements moved into North America and eventually, into Europe via transatlantic connections. Later, a marsupial traveled to South America from Australia or Antarctica, transporting the forebears of a genus of pygiopsyllid. The Insectivora arose in Asia and entered North America without fleas or lice. The monophyetic Order Siphonaptera must date back to the Jurassic and existed on parts of Pangea, at least as ancestral hystrichopsyllids, and certain families or subfamilies arose in components of Gondwanaland and others in Laurasia,as indicated, e.g. Pygiopsyllidae in Australia, Pulicidae in Africa, etc. The Anoplura arose in North America, perhaps in Early Paleocene.

There were African/South American faunal connections, by rafting, in the Early Eocene, involving "hystrichomorph" rodents and ancestral ceboid monkeys and their ectoparasites, e.g. polyplacid lice of phiomorph and caviomorph rodents; ctenophthalmine fleas; and perhaps Pediculus Anoplura. Virological and other parasitological evidence also suggest the possibility of such faunal relationships. The data on Anoplura indicate that the ultimate roots of the murids go back to the Asian mainland, even if rats as such arose in Wallacea or southeast Asian islands. Regardless, Rattus is a relatively youthful taxon and moved from Southeast Asia towards Australia, and transported some fleas of Palearctic derivation. On movements in the opposite direction, they carried pygiopsyllids. Penetration by sciurids into Borneo, Sulawesi, etc. was subsequent to that of some murids. Madagascar was originally much further north that at present, probably opposite Somalia, as indicated by their cricetid rodents and leptopsyllid fleas of Palearctic origin, and by the dearth of native murids and their ectoparasites. The distribution of fleas like Odontopsyllus and some hystrichopsyllids suggest that direct transalantic connections formerly existed between Europe and North America, but the absence of such data for the ceratophyllids, a more recently evolved group, indicates the corridor was terminated after the Eocene. The Pediculus and Pthirus lines of human lice may antedate the divergence of the humanoid and anthropod branches."

3. Publications By These Investigators

a. Two articles on basic, experimental studies on the immunological aspects of R. mooseri-host inter-relationships, using the infant and adult rat as a laboratory model are ready for submission for publication (Arango-Jarmillo et al, A & B, in prep.) The long paper on the zoogeography of some mammals and their lice and fleas, mentioned just above (*#Traub et al, 1980, in press) is being published in a volume edited by that author. Included therein also is a paper (*#Traub et al, 1980, in press) which summarizes our views on the ecology of murine typhus, and stresses the potential importance of dust-borne, infected feces of fleas and lice as a source of murine typhus infection. It is pointed out that ectoparasites that do not bite man may nevertheless prove to be important factors in transmission by means of infective rickettsiae in their feces. New and significant data and observations have been forthcoming at such a rapid rate regarding the studies on murine typhus that manuscripts have become obsolete or inadequate before they could be submitted for publication. However, we now are at the stage where articles can be written on the Ethiopian studies, and these are in preparation.

b. There have been some recent publications prepared by the Responsible Investigator and members of this Department that are directly pertinent to the work being done under this Contract but which represent sponsorship by non-Navy sources. They are mentioned for documentation, for purposes of completeness regarding current state of the art, and so that the bibliography cited in this report is up to date and suitable for reference. As in the case of other relevant work done under other auspices by our staff, the items marked with a #, and are as follows: An article on the mechanisms of immunity in R. mooseri infection has appeared (#Murphy et al, 1979A), and the characterization of the antibody response to R. mooseri erythrocyte sensitizing substance was discussed in a later paper (Murphy et al 1979B). The ultra-structure of typhus and other rickettsiae was treated by #Silverman and Wisseman (1979), and another paper dealt with a staining technique for emmerating rickettsiae in yolk sac (#Silverman et al, 1979). An invitational lecture by #Wisseman on the prevention and control of rickettsial diseases was published in 1978. #Myers et al (1978) reported on the absence of hydrogen peroxide production in R. prowazeki.

5. Summary of Progress Report

a. Studies on the ecology of murine typhus in Ethiopia strongly suggest that: 1) Commensal Rattus indoors are deeply implicated in the natural history of this zoonosis, as are Xenopsylla cheopis, X. bantorum and Leptopsylla segnis fleas, and rat-lice (Polyplax and Hoplopleura) 2) Sylvan and campestral rodents outdoors are not involved, even when living a few yards from known endemic foci. 3) Hyperendemic minifoci (e.g., a single building) exist wherein a very large proportion of the Rattus, Xenopsylla and Leptopsylla fleas and rat lice are infected with R. mooseri, the etiological agent of murine typhus. 4) The evidence indicates that within the minifocus there is a highly circumscribed "microfocus" where the various factors inter-act, and the Rattus nest seems to be the most logical candidate in that regard. 5) Native murine (e.g. Arvicanthis, Praomys, etc.) entering the minifocus from the outdoors and perhaps even living as a commensal in the edifice may become infected but if so, it seems to be a peripheral phenomenon and the infection does not seem to become established outside in the more normal habitat of such rodents.

b. The observations on murine typhus in Burma are falling into the same pattern, but with somewhat different participants, yet still strongly centered around commensal Rattus (especially R. rattus and R. norvegicus) but perhaps R. exulans also, and Xenopsylla cheopis fleas. The only other common flea on peridomestic small mammals (theraphions) is X. astia, while 2 of the 3 rat lice were not found in Ethiopia. The house mouse, Mus musculus, Bandicota bengalensis, and the shrew Suncus murinus are also common indoors. All of these mammals and ectoparasites have now been found (by fluorescent antibody tests) naturally infected with R. mooseri in Rangoon. A few mesostigmatid mites from rats and 2 of 3 Bandicota indica were also positive.

c. The observations in Burma also support the concept of the rat nest as a hyperendemic microfocus of murine typhus, e.g. young rats have almost as high a rate of R. mooseri infection as old ones. Presumably they are infected before they leave the nest.

d. It has been demonstrated that clinical murine typhus, classified as "pyrexia of unknown origin", occurs in Rangoon, and in a human sero survey (by indirect fluorescent antibody tests), 22% of those tested thus far have evidence of prior R. mooseri infection.

e. There is a tremendous potential for research on murine typhus in Burma. The Government is much interested in our program and is now permitting our collaborators from WHO to work in areas that were formerly closed to them. We hope we can obtain data on such important points as the possible role of sylvan and campestral rodents; the effect of the type of housing upon the incidence of scrub typhus in man, etc.

f. Basic studies on experimental R. mooseri infection in infant and adult rats in Baltimore have reinforced our views about the potential role of the rat nest in the ecology of this rickettsiosis. Baby rats were found to be extremely susceptible to infection but show no signs of illness. Moreover, their immunological response is the same as adults.

g. With the partial support of this Contract, a large paper on the zoogeography of rodents, insectivores, fleas and lice has been prepared (Traub 1980 in press) which contributes to the understanding of the distribution of certain vectors and reservoirs of disease.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

a. Studies on the ecology of murine typhus in Ethiopia strongly suggest that: zoonosis, as are Xenopsylla cheopis, X. bantorum and Leptopsylla segnis fleas, are rat-lice (Polyplax and Hoplopleura) 2) Sylvan and campestral rodents outdoors are not involved, even when living a few yards from known endemic foci. 3) Hyperendemic minifoci (e.g., a single building) exist wherein a very large proportion of the Rattus, Xenopsylla and Leptopsylla fleas and rat lice are infected with R. mooseri, the etiological agent of murine typhus. 4) The evidence in-

dicates that within the minifocus there is a highly circumscribed "microfocus" where the various factors inter-act, and the Rattus nest seems to be the most logical candidate in that regard. 5) Native murine (e.g. Arvicanthis, Praomys, etc.) entering the minifocus from the outdoors and perhaps even living as a commensal in the edifice may become infected but if so, it seems to be a peripheral phenomenon and the infection does not seem to become established outside in the more normal habitat of such rodents.

b. The observations on murine typhus in Burma are falling into the same pattern, but with somewhat different participants, yet still strongly centered around commensal Rattus (especially R. rattus and R. norvegicus) but perhaps R. exulans also, and Xenopsylla cheopis fleas. The only other common flea on peridomestic small mammals (theraphions) is X. astia, while 2 of the 3 rat lice were not found in Ethiopia. The house mouse, Mus musculus, Bandicota bengalensis, and the shrew Suncus murinus are also common indoors. All of these mammals and ectoparasites have now been found (by fluorescent antibody tests) naturally infected with R. mooseri in Rangoon. A few mesostigmatid mites from rats and 2 of 3 Bandicota indica were also positive.

c. The observations in Burma also support the concept of the rat as a hyperendemic microfocus of murine typhus, e.g. young rats have almost as high a rate of R. mooseri infection as old ones. Presumably they are infected before they leave the nest.